Simple Recruitment Model Describes Control of Conditioned Nictitating Membrane Responses by Retractor Bulbi Muscle

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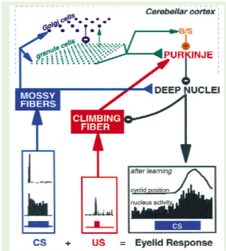
1 Introduction

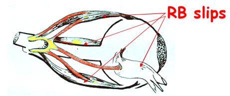
How does the cerebellum produce precisely timed and appropriately shaped conditioned eyeblink responses?

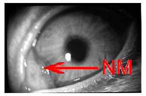
View #1: Simple linear control
Many models assume that the position of the external eyelid or nictitating membrane is a simple linear reflection of activity in the deep cerebellar nuclei (e.g. [Medina and Mauk, Nature Neurosci. 3 (2000) 1205]).

View #2: Complicated nonlinear dynamics
"it is somewhat unlikely that the actual discharge rate of interpositus neurons could be correlated with… the nictitating membrane displacement, as this is a passive, highly damped movement" [Delgado-García and Gruart, Brain Res. Rev. 49 (2005) 367-376].



2 Background: The nictitating membrane response system

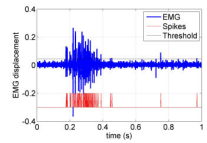




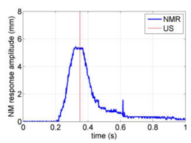
The four slips of the retractor bulbi (RB) muscle contract to pull the globe back into the orbit.

The retracting globe pushes against Harder's gland, which slides to move the nictitating membrane (NM) across the globe.

A typical EMG recording of muscle activity from an inserted electrode is (extracted MN spikes also shown):

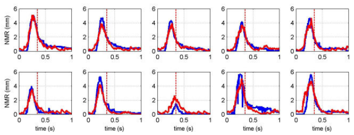


A typical NM response is:



3 Result: Linearity

A simple *linear* model accurately reproduces the output topography of the eyeblink system from EMG spike input.



CR data in blue; model response in red.
Results for dataset #4.

Model is a first order linear filter, with two parameters:
(i) a *time constant* t_0 for the decay of the response
(ii) a *gain* for the response from a single input spike.

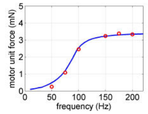
The linear modelling approach (View #1) appears correct. Eyeblink conditioned response (CR) position linearly reflects input motoneuron activity inferred from the EMG.

This presents the cerebellum with a simplified view of the output system that eases control of the response profile and its timing.

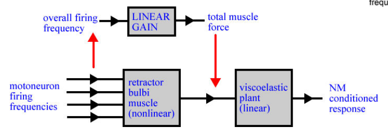
4 Question: How is linearity achieved?

How is the system linearised in practice, considering the underlying muscle dynamics are nonlinear?

e.g. The force-frequency relation for a single motor unit has the characteristic nonlinear sigmoid shape shown in the figure.



But an implication of the linear model (slide #3) is that overall firing frequency is proportional to total muscle force. It is this relation that is linear, not that for a single motor unit:

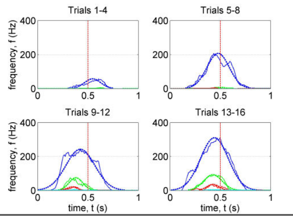


Somehow the system appears to be using motor unit recruitment to generate overall linearity. Examine this recruitment strategy with EMG spike height…

5 Spike height properties 1

Spikes in the EMG are assumed to correspond to motoneuron firing. These spikes can be separated into populations by EMG height (e.g. small, medium and large spikes).

Spike height populations display a remarkable amount of regularity. They:
(i) Fit Gaussian profiles to very high accuracy
(ii) Have a clear *recruitment strategy* where small spikes always appear before larger ones.



Small spikes
Medium spikes
Large spikes
Dataset #1 shown

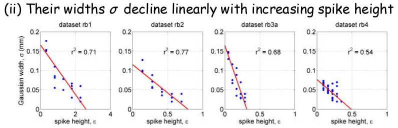
$$f(t) = h\exp\left[\frac{-(t-\mu)^2}{2\sigma^2}\right],$$

6 Spike height properties 2

The Gaussians in slide #5 have the following properties:

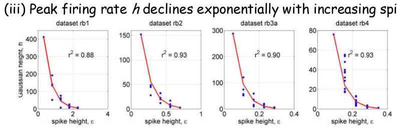
(i) Their means μ are timed to the US onset independently of spike height.

(ii) Their widths σ decline linearly with increasing spike height ε.



$$\sigma \propto \varepsilon_{\max} - \varepsilon$$

(iii) Peak firing rate h declines exponentially with increasing spike height ε.



$$h_i \propto \exp(-\alpha\varepsilon_i)$$

This striking regularity suggests a simple principle generates motoneuron firing & recruitment from some common input.

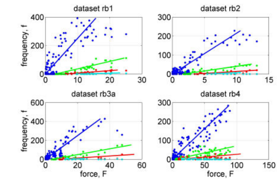
7 Inferred force and common drive 1

Consider how muscle force relates to EMG spike frequency for the individual spike height populations.

Muscle force can be inferred from running the CR profile x(t) back through the visco-elastic plant (see slide #4) using

$$F(t) \propto \dot{x} + x/t_0$$

Remarkably, each EMG spike height population displays linearity between its spike frequency and the *total* muscle force F(t):



Small spikes
Medium spikes
Large spikes

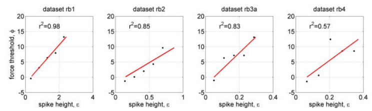
$$F(t) = m_i^{-1} f_i(t) + \varphi_i, \quad f_i \geq 0$$
$$\Updownarrow$$
$$f_i(t) = m_i\left[F(t) - \varphi_i\right]_+$$

Thus a signal linearly related to total muscle force could represent a common drive input to the system.

8 Inferred force and common drive 2

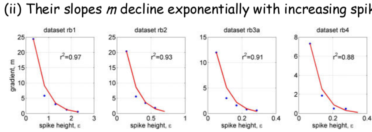
The force/common drive plots in slide #7 have the following properties:

(i) Their thresholds φ increase linearly with spike height ε (these thresholds are the x-intercepts below which no spikes occur).



$$\varphi \propto \varepsilon - \varepsilon_{\min}$$

(ii) Their slopes m decline exponentially with increasing spike height ε.



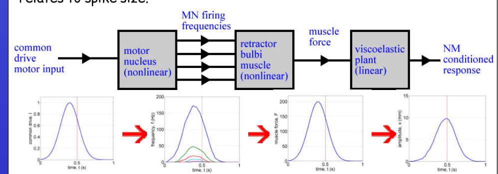
$$m \propto \exp(-\alpha\varepsilon)$$

This further regularity reinforces that the system dynamics are generated from a common input controlling muscle force.

9 Biophysical model of system

Construct a simple, biologically realistic model of the system that displays all the above features. Use this model to identify the form of the common input.

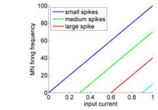
(i) Suppose the system has a common motor drive. Consider a Gaussian profile for this single input.
(ii) Then a set of spike height dependent thresholds are used to construct the individual motoneuron recruitment and firing patterns from this drive.
(iii) The MN firing frequencies are fed into a biologically realistic model of the RB muscle and viscoelastic plant to obtain the CR profile [Bartha and Thompson, Biol. Cybern. 68 (1992) 135-144,145-154]. Motor unit strength relates to spike size.



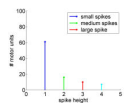
10 Model results: predicted EMG

This model reproduces EMG features in slides #5-6.

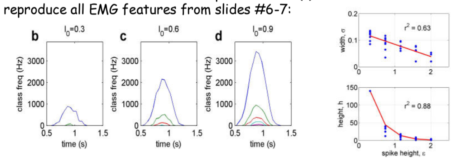
• Take: (i) motoneuron firing frequencies to be proportional to the common drive current I(t), with thresholds θ increasing linearly with spike height; (ii) motor unit population # n_i decreasing exponentially with spike height.



$$f_i(t) = k\left[I(t) - \theta_i\right]_+$$
$$k \text{ const}, \quad \theta_i \propto \varepsilon$$
$$n_i \propto \exp(-\alpha\varepsilon)$$



• Then a Gaussian common drive input current I(t) leads to results that reproduce all EMG features from slides #6-7:

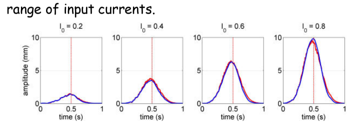


11 Model results: predicted response

The biophysical model with a common motor drive reproduces the linearity of the biological system.

• Take: motor unit force as proportional to EMG spike height and the firing frequencies distributed as in slide #10.

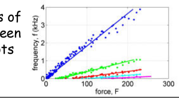
• Then a Gaussian common drive leads to realistic NM responses for a range of input currents.



Cf slide #3: linear model in red; biophysical model in blue.

An emergent model property is that it is *highly linear* - a very important feature for the control of the system.

• Also note that repeating the analysis of slides #7-8 gives similar results between inferred force and MN frequency (plots for slide #8 not shown)



12 Conclusions

Our results are consistent with:

COMMON DRIVE: All motoneurons receive a common drive, which for conditioned responses has a Gaussian profile.

RECRUITMENT: Motoneurons controlling weak motor units have lower thresholds than those controlling strong motor units (cf size principle). The Gaussian input then ensures that the many weak motor units are recruited before the few stronger units.

LINEARITY: Recruitment linearises the system such that: (i) The common drive is proportional to total muscle force. (ii) The peak drive is proportional to peak response amplitude, and its timing is proportional to peak response time.

CONTROL: Linearity gives the cerebellum a simplified view of the output system that eases control of response topography. The cerebellum outputs a Gaussian common drive whose peak linearly controls the peak response amplitude and timing.